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**REMARKS**

Applicants have studied the Office Action mailed February 26, 2004 and have made amendments to the specification and claims. It is respectfully submitted that the application, as amended, is in condition for allowance. Reconsideration and allowance of the pending claims in view of the above amendment and following remarks is respectfully requested.

**Priority:**

The Examiner noted that the filing date of the 60/157,832 provisional application in the first line of the specification is incorrect.

Applicants have hereby deleted the reference to the 60/157,832 provisional application from the first line of the specification. Applicants no longer claim benefit of provisional application 60/157,832 in the instant application.

**Specification:**

The Examiner stated that the title of the invention is not descriptive of the elected invention.

Applicants have hereby amended the title, as indicated above.

**Declaration/Application Data Sheet:**

The Examiner stated that the declaration is defective because it includes an incorrect filing date for provisional application 60/157,832, and stated that a new declaration in compliance with 37 CFR 1.67(a) is required.

Applicants no longer claim benefit of provisional application 60/157,832 in the instant application.

MPEP 602.01 states that, "...in some cases, a deficiency in the oath or declaration can be corrected by a supplemental paper such as an application data sheet...and a new oath or declaration is not necessary." Accordingly, in light of the difficulties associated with contacting the inventors of the instant application (three of whom are no longer with

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the company) to have them execute a new declaration, Applicants hereby respectfully request that the Examiner accept an Application Data Sheet in lieu of a new declaration in order to correct the defect in the declaration cited by the Examiner.

In view of this request, Applicants hereby submit an Application Data Sheet that correctly sets forth the provisional applications which the instant application claims benefit of. Specifically, because benefit of provisional application 60/157,832 is no longer claimed in the instant application, provisional application 60/157,832 is not cited on the Application Data Sheet submitted herewith.

**Rejection under 35 USC §101 (Non-Statutory Subject Matter):**

The Examiner rejected claims 1, 5, 9, and 13 under 35 U.S.C. §101 as being directed to non-statutory subject matter. In making this rejection, the Examiner asserts that the claims as written can be interpreted to cover naturally occurring products.

Applicants have hereby amended claims 1, 5, 9, and 13 to clarify that they are intended to encompass non-naturally occurring detection reagents, rather than any products as they exist in nature.

**Rejections under 35 USC §101 and §112, 1st paragraph (Utility):**

The Examiner rejected claims 1-16 under 35 U.S.C. §101 and §112, 1st paragraph, as not supported by either a specific, substantial and credible utility or a well established utility and, consequently, one skilled in the art would not know how to use the claimed invention.

In making these rejections, the Examiner states that the disclosed uses are generally applicable to broad classes of this subject matter and further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. The Examiner states that the uses asserted in the specification are general utilities and uses in further research that are applicable to virtually any group of predicted transcripts or predicted ORFs. The Examiner states that experiments might eventually result in the identification of, e.g., a particular expression pattern or set of sequences or polymorphisms associated with a particular condition or genetic defect, such general

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research methods do not constitute substantial uses that are specific to the group of molecules claimed by applicant, and the Examiner states that the sequences elected by Applicant appear to constitute a group of the first 1000 predicted transcripts identified in the *D. melanogaster* genome, rather than e.g., a specific group of actual transcripts associated with (and thereby useful in detecting) a specific condition or state. The Examiner states that not only would further experimentation be required to establish some type of specific use for the group of sequences elected by Applicant (if such a use even exists), but additional research would be required to establish that this group of sequences are actually transcribed in the manner predicted by Applicant. The Examiner reiterates that further research and experimentation on nucleic acids or a group thereof constitutes a generally utility, rather than a specific and substantial "real world" use. The Examiner states that the prior art does disclose useful arrays but to the extent that the claims are drawn to the particular sequences elected by Applicant, the prior art does not disclose any type of specific use for this group of predicted transcripts, and thus the prior art does not provide any evidence of a well-established utility for the elected invention. The Examiner concludes by stating that Applicant should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

In response, Applicants respectfully assert that invention as claimed in claims 1-16 is supported by patentable utilities, particularly well established utilities.

The Examiner has stated, for example, that "the sequences elected by Applicant appear to constitute a group of the first 1000 predicted transcripts identified in the *D. melanogaster* genome, rather than e.g., a specific group of actual transcripts associated with (and thereby useful in detecting) a specific condition or state" (lines 8-12 on page 6 of the 2/26/04 Office Action). The Examiner has also stated that "...to the extent that the claims are drawn to the particular sequences elected by Applicant, the prior art does not disclose any type of specific use for this group of predicted transcripts, and thus the prior art does not provide any evidence of a well-established utility for the elected invention" (lines 5-9 on page 7 of the 2/26/04 Office Action).

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However, Applicants have not elected a group of the first 1000 predicted transcripts identified in the *D. melanogaster* genome. Rather, Applicants have elected a group of sequences that constitute substantially all of the predicted transcripts identified in the *D. melanogaster* genome as of the filing date of the instant application. Applicants have elected the 14,336 transcript sequences identified as "SEQ ID NOS:2, 5, 8, 11...43001, 43004, 43007" (every 3<sup>rd</sup> sequence; see part '4' below in response to the rejections under 35 USC §112, 2nd paragraph). The claims are drawn to detection reagents (e.g., arrays) comprising at least any 1000, 2000, 5000, or 10,000 (claims 1, 5, 9, and 13, respectively) of these 14,336 transcripts.

The invention as claimed in claims 1-16 is amenable to a wide variety of utilities that are well established in the art, depending on how the array or other detection reagent is configured (e.g., which groups of at least 1000, 2000, 5000, or 10,000 transcripts, selected from amongst the 14,336 transcripts elected by Applicants, are implemented in the detection reagent), and one skilled in the art would know how to configure the detection reagent based on their intended use. The groups of at least 1000, 2000, 5000, or 10,000 transcripts, which the array or other detection reagent comprises, can be selected from amongst, for example, transcripts that encode proteins of specific protein families (e.g., enzymes such as proteases, kinases, phosphatases, etc.), transcripts which are encoded by *Drosophila* orthologs of known human disease genes or known human drug target genes, transcripts involved in various *Drosophila* biological pathways, etc., wherein the transcripts are selected from amongst the 14,336 transcripts elected by Applicants. Detection reagents such as these have well established utilities in the art.

Given the sequences of substantially all of the predicted transcripts identified in the *D. melanogaster* genome, as provided in the instant application (SEQ ID NOS:2, 5, 8, 11...43001, 43004, 43007), one skilled in the art would know how to select which groups of at least 1000, 2000, 5000, or 10,000 of these transcripts to include in the detection reagent depending on the intended use of the detection reagent.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-16 under 35 U.S.C. §101 and §112, 1st paragraph.

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**Rejections under 35 USC §112, 2nd paragraph:**

1) The Examiner rejected claims 1-16 under 35 U.S.C. §112, 2nd paragraph, as being indefinite over the recitation of the limitation "capable of detecting" in claims 1, 5, 9, and 13. The Examiner states that capability is a latent characteristic.

Applicants have hereby amended claims 1, 5, 9, and 13 for clarity by removing the "capable" language.

2) The Examiner rejected claims 1-16 under 35 U.S.C. §112, 2nd paragraph, as being indefinite over the recitation of the phrase "wherein each of at least"

1000/2000/5000/10,000 "of said Drosophila transcripts consists of a nucleotide sequence selected from the group consisting of..." in claims 1, 5, 9, and 13, respectively, because it is unclear from this language as to whether the claims encompass reagents that are "capable of detecting" at least 1000/2000/5000/10,000 copies of the same transcript, or whether the claims require a reagent that is "capable of detecting" at least 1000/2000/5000/10,000 different transcripts selected from the recited molecules.

Applicants have hereby amended claims 1, 5, 9, and 13 to clarify that the claims are intended to encompass a reagent that is "capable of detecting" at least 1000/2000/5000/10,000 different transcripts selected from the recited molecules.

3) The Examiner rejected claims 1-16 under 35 U.S.C. §112, 2nd paragraph, as being indefinite over the recitation of the phrase "the transcript sequences of SEQ ID NOS:2, 5, 8, 11...43001, 43004, 43007" in claims 1, 5, 9, and 13 because it is unclear from this language as to whether the claims require the particular sequences set forth in the recited SEQ ID NOS (i.e., the full-length sequences), or whether the claims encompass subsequences of the recited SEQ ID NOS.

In response, Applicants respectfully assert that the "consisting" language used in claims 1, 5, 9, and 13 to describe the recited SEQ ID NOS ("...wherein each of at least" 1000/2000/5000/10,000 "of said Drosophila transcripts consists of a nucleotide sequence selected from the group consisting of the transcript sequences of SEQ ID NOS:2, 5, 8, 11

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... 43001, 43004, 43007...") makes it clear that the claims are definite and are directed to the particular full-length sequences set forth in the recited SEQ ID NOS.

4) The Examiner rejected claims 1-16 under 35 U.S.C. §112, 2nd paragraph, as being indefinite over the recitation of the limitation "SEQ ID NOS:2, 5, 8, 11...43001, 43004, 43007" in claims 1, 5, 9, and 13 because this recitation does not make clear which particular sequences are encompassed by the claims.

Applicants hereby assert that the limitation "SEQ ID NOS:2, 5, 8, 11...43001, 43004, 43007" is intended to refer to every 3<sup>rd</sup> sequence beginning with SEQ ID NO:2 and ending with SEQ ID NO:43007, inclusive (a total of 14,336 sequences). Thus, for example, SEQ ID NOS:14, 17, 20, 23, 26, 29, 32, and so on, are included. Further, SEQ ID NOS:42980, 42983, 42986, 42989, 42992, 42995, 42998 are also included, as well as every 3<sup>rd</sup> sequence between SEQ ID NO:32 and SEQ ID NO:42980, inclusive. Because the arrangement of the sequences in the Sequence Listing (and in Table 1) is in the repetitive format of "genomic sequence - transcript sequence - protein sequence", every third sequence beginning with the second sequence is a transcript sequence. Accordingly, the nomenclature "SEQ ID NOS:2, 5, 8, 11...43001, 43004, 43007" is used in the claims to refer to the 14,336 transcript sequences, which occur in the Sequence Listing as every 3<sup>rd</sup> sequence (beginning with SEQ ID NO:2).

5) The Examiner rejected claims 3-4, 7-8, 11-12, and 15-16 under 35 U.S.C. §112, 2nd paragraph, as being indefinite over the recitation of the phrase "wherein said array is comprised of..." because it is unclear whether this language requires an array that is constructed from ("comprised of") oligonucleotides/polynucleotides, or whether the claims are intended to encompass an array that comprises oligonucleotides/polynucleotides.

Claims 3-4, 7-8, 11-12, and 15-16 have hereby been amended to clarify that the claims are intended to encompass an array that comprises oligonucleotides/polynucleotides.

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6) The Examiner rejected claims 3-4, 7-8, 11-12, and 15-16 under 35 U.S.C. §112, 2nd paragraph, as being indefinite over the recitation of the phrase “wherein each of said” oligonucleotides/polynucleotides “is fully complementary to one of said *Drosophila* transcripts” because it is unclear whether the claims require an array comprising multiple copies of a single oligonucleotide/polynucleotide that is “fully complementary to one” of the multitude of previously recited transcripts, or whether the claims are intended to encompass multiple different oligonucleotides/polynucleotides, each of which is fully complementary to a different one of the recited transcripts. The Examiner also notes that the claims previously refer to both a group of 1000/2000/5000/10,000 “or more *Drosophila* transcripts” and to a subset of “at least” 1000/2000/5000/10,000 of said transcripts, and it is not clear which of these groups constitutes “said *Drosophila* transcripts” as recited in claims 3-4, 7-8, 11-12, and 15-16.

The amendments hereby made to claims 1, 5, 9, and 13 to clarify that the claims are intended to encompass a reagent that is “capable of detecting” at least 1000/2000/5000/10,000 different transcripts selected from the recited molecules (as discussed above in part 2 of rejections under 35 USC §112, 2nd paragraph) inherently clarifies that the oligonucleotides/polynucleotides recited in dependent claims 3-4, 7-8, 11-12, and 15-16 must collectively be “capable of detecting” at least 1000/2000/5000/10,000 different transcripts selected from the recited molecules, thereby making claims 3-4, 7-8, 11-12, and 15-16 definite.

However, to clarify, this does not necessarily mean that each of the oligonucleotides/polynucleotides of the array must be fully complementary to a different transcript (for example, if desired, each of the oligonucleotides/polynucleotides of the array can be fully complementary to a different transcript). For example, in order to increase the accuracy of gene expression analysis, it is common in the art to include multiple probes (e.g., oligonucleotides/polynucleotides) on the same array which are each designed so as to specifically hybridize to the same transcript (although, if desired, each probe may be designed so as to hybridize to a different region of the same transcript). As a specific example, an array that is capable of detecting 1000 different transcripts could comprise 2000 oligonucleotides/polynucleotides, wherein each different transcript is

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targeted by two different oligonucleotides/polynucleotides which specifically hybridize to that transcript (and each of these two oligonucleotides/polynucleotides may be optionally designed so as to hybridize to a different region of the same transcript).

Claims 3-4, 7-8, 11-12, and 15-16 have also hereby been amended to clarify that the subset of at least 1000/2000/5000/10,000 *Drosophila* transcripts constitutes "said *Drosophila* transcripts" as recited in claims 3-4, 7-8, 11-12, and 15-16.

7) Examiner rejected claim 16 under 35 U.S.C. §112, 2nd paragraph, as being indefinite, and the Examiner noted that it appears that claim 16 may have been intended to depend from claim 14, rather than claim 15.

Claim 16 has hereby been amended to depend from claim 14 rather than claim 15.

**Rejections under 35 USC §102:**

1) The Examiner rejected claims 1-3, 5-7, 9-11, and 13-15 under 35 U.S.C. §102(b) as being anticipated by Brennan (U.S. Patent 5,474,796 A [12/1995]). Brennan discloses an array of oligonucleotides comprising all possible 10-mers.

Applicants have hereby amended claims 1, 5, 9, and 13 to clarify that the claimed detection reagents exclusively detect the presence of 1000/2000/5000/10,000 or more different specific *Drosophila* transcripts. In contrast, the array of Brennan et al. will inherently detect a wide variety of transcripts and related molecules other than the specific *Drosophila* transcripts detected by the claimed detection reagents. Therefore, the array of Brennan et al. does not anticipate claims 1-3, 5-7, 9-11, and 13-15.

2) The Examiner rejected claims 1-2, 5-6, 9-10, and 13-14 under 35 U.S.C. §102 as being anticipated by Bryant et al. (Proceedings of the National Academy of Sciences USA 96:5559-5564 [5/1999]). Bryant et al. disclose a microarray comprising "4,500 unique *Drosophila* cDNAs".

Applicants respectfully assert that, based on the information provided in the Bryant et al. reference (Proceedings of the National Academy of Sciences USA 96:5559-5564 [5/1999]), Bryant et al. does not anticipate claims 1-2, 5-6, 9-10, and 13-14. It is



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only apparent from the Bryant et al. reference that Bryant et al. used a microarray comprising "4,500 unique Drosophila cDNAs". However, apparently no information is provided regarding the sequences of these "4,500 unique Drosophila cDNAs". Claims 1-2, 5-6, 9-10, and 13-14 are not directed to detection reagents for detecting *any* 1000/2000/5000/10,000 Drosophila transcripts, but rather are directed to detection reagents for detecting Drosophila transcripts that consists of specific sequences (e.g., SEQ ID NOS:2, 5, 8, 11 . . . 43001, 43004, 43007). Without knowledge of the specific sequences of the "4,500 unique Drosophila cDNAs" of Bryant et al.'s microarray, and thus the specific sequences of the Drosophila transcripts that Bryant et al.'s microarray will detect, Bryant et al. can not be considered to anticipate claims 1-2, 5-6, 9-10, and 13-14.

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### Conclusions

By way of the above amendments, claims 1, 3-5, 7-9, 11-13, and 15-16 have been amended. As such, claims 1-16 remain pending.

Support for the amendments to the claims can be found in the specification, Table 1, and/or the Sequence Listing. The amendments to the claims add no new subject matter and their entry is respectfully requested.

In view of the above amendment and remarks, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the objections and rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent at (240) 453-3812 should the Examiner believe a telephone interview would advance prosecution of the application.

Respectfully submitted,

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